39. The method of claim 38, wherein the polynucleotide comprises a sequence selected from the group consisting of
GATTGCCTGACGTCAGAGAG (SEQ ID NO:8),
TCGATCGGGGCGGGGCGAGC (SEQ ID NO:12),
AGCGGGGGCGAGCGGGGGCG (SEQ ID NO:14),
GTCCATTTCCCGTAAATCTT (SEQ ID NO:16),
CTGATTTCCCCGAAATGATG (SEQ ID NO:19),
AAGCGAAAATGAAATTGACT (SEQ ID NO:22), and
CAGGCATAACGGTTCCGTAG (SEQ ID NO:23).

Substitute Sequence Listing

Included herewith are a copy of a Notice to Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, a substitute Sequence Listing, substitute computer readable form (CRF) copy of the Sequence Listing, and an accompanying statement under 37 C.F.R. § 1.821(g). These are submitted in response to the specific request of the Examiner.

Remarks

Claims 1-23 were rejected. Pending claims 1-23 are cancelled. New claims 24-39 are presented. Corrections are made to ten typographical errors in the specification. A substitute Sequence Listing and computer readable form copy of the substitute Sequence Listing is provided. No new matter is introduced.

The following remarks address the rejections and comments of the Examiner, directed to cancelled claims 1-23, as they may apply to the newly presented claims 24-39.

Typographical corrections are made in ten places in the specification, including those noted by, and related to those noted by, the Examiner, without changing the meaning or content of the application. The changes on pages 12 and 16 are related to claim objections made by the Examiner. No new matter is introduced by these typographical corrections.

Multiple dependent claims 4-22 are canceled. Newly presented claims are drafted in independent and singly dependent form.

Claims 19-22, rejected under 35 U.S.C. § 101, are canceled.

Claim Rejections Under 35 U.S.C. § 112

Claims 9, 12, 15, and 18-22 were rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 9, 12, 15, and 18-22 are canceled, and the comments directed to claims 8, 9, 12, and 18-22 are no longer applicable. As to an antigen selected from the group comprising, among others, a "tumor cell" in claim 15, applicant refers Examiner to page 12, line 18, for support of this claim language. Newly presented claims 27 and 32, now most closely corresponding to claim 15, retain this language and further include "tumor antigen" as suggested by the Examiner and as supported on page 12, line 30.

Claims 1-18 were rejected by the Examiner under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Newly presented claims no longer contain the language "parts of the sequences," "a motif of a transcription factor binding site," "derived from a eukaryotic binding site," or "non-toxic derivative of a polynucleotide." The newly presented claims recite particular nucleotide sequences, which are disclosed on page 17, line 6, and in Table 4 on page 25.

Applicant believes the newly presented claims conform to 35 U.S.C. § 112, first and second paragraphs. In view of the above, the applicant respectfully requests the Examiner to withdraw her rejections under 35 U.S.C. § 112, first and second paragraphs.

Claim Rejections Under 35 U.S.C. § 102

Claims 1-6, 9, 11, 12, 16, 17, 19, and 20 were rejected under 35 U.S.C. § 102(e) as being anticipated by Henderson (US Patent No. 6,057,299). Claims 1-6, 9, 11, 12, 16, 17, 19, and 20

are canceled. Henderson was filed on September 27, 1996 and claims priority back to June 27, 1995. The instant application was filed as a PCT application on January 23, 1998, and claims priority back to January 23, 1997. The Examiner's rejection over Henderson on the basis of 35 U.S.C. § 102(e) is not traversed on the basis of these dates alone.

However, the applicant respectfully traverses the Examiner's rejection on the basis of Henderson because it appears the Examiner has misunderstood what Henderson actually teaches. According to the Examiner, Henderson teaches "pharmaceutical compositions comprising an antigen, a polynucleotide which comprises a binding site for a eukaryotic transcription factor, and a diluent ... and which composition is used for a vaccine for the treatment of cancer, and which vaccine results in the modulation of an immune response."

The Henderson reference is directed specifically to DNA sequences within or flanking a gene which is preferentially expressed in prostate cells which function to enhance or drive transcription of the cis-linked gene in prostate cells, i.e., prostate-specific transcriptional regulatory sequences. Column 12, lines 32-37; column 17, line 22, through column 18, line 23; as well as throughout the reference. In particular, the Henderson reference teaches placing a toxin gene under the control of a prostate-specific transcriptional regulatory sequence in an expression vector. Column 14. line 35, through column 16, line 36. In an alternative embodiment (column 16, lines 38-64), Henderson teaches placing a gene encoding a lymphokine or antigen under the control of a prostate-specific transcriptional regulatory sequence in an expression vector. In this latter embodiment, the expressed lymphokine or antigen potentiates or elicits an immune response directed against prostate cells expressing the lymphokine or antigen. Column 16, lines 39-48. In a further embodiment, the Henderson reference teaches an antisense sequence of at least 30 bp and usually at least 50 bp, targeting the coding region of an essential gene for the proliferation or viability of the host. Column 17, lines 22-41.

In view of the above, applicant finds first that the Henderson reference does not teach the use of transcriptional regulatory sequences apart from prostate-specific transcriptional regulatory sequences. In contrast, specific sequences in newly presented claims 24-39 correspond to binding sites for the following transcription factors: SEQ ID NO:8, CRE; SEQ ID NO:9, IL-13; SEQ ID NO:10, IL-12 p40; SEQ ID NO:11, AP-1; SEQ ID NO:12, SP-1; SEQ ID NO:13, C/EBP; SEQ ID NO:14, EGR; SEQ ID NO:16, SIE; SEQ ID NO:17, STAT1; SEQ ID NO:19, STAT4; SEQ ID NO:20, STAT5; SEQ ID NO:21, STAT5/6; SEQ ID NO:22, IRF-1; and SEQ

ID NO:23, c-Myb. None of these sequences is a prostate-specific transcriptional regulatory sequence.

Applicant finds second that the Henderson reference does not teach that the prostate-specific transcriptional regulatory sequence is immunomodulatory itself. Rather, Henderson teaches that the lymphokine or antigen expressed under the control of the prostate-specific transcriptional regulatory sequence is immunomodulatory. In contrast, the instant application teaches that the polynucleotide comprising a sequence of a binding site for a transcription factor is immunomodulatory itself.

Third, applicant finds that the Henderson reference does not teach the use of sense polynucleotides of less than 30 bp, targeting a non-coding binding site for a transcription factor. As noted above, Henderson specifically teaches the use of antisense sequence of at least 30 bp, targeting the coding region of an essential gene for the proliferation or viability of the host. In contrast, the claimed polynucleotide sequences are 18-20 bp long, are not required to be antisense, and are targeted to non-coding binding sites for particular transcription factors.

In summary with regard to the Henderson reference, applicant finds the Examiner appears to have misunderstood the actual teachings of the Henderson reference, and therefore respectfully requests the Examiner to withdraw her 102(e) rejection over Henderson.

Claim 23 was rejected by the Examiner under 35 U.S.C. § 102(e) as being anticipated by Watson (US Patent No. 5,912,168). Claim 23 is canceled. Watson was filed on August 30, 1996 and has no earlier priority claim. The instant application was filed as a PCT application on January 23, 1998, and claims priority to January 23, 1997. The Examiner's rejection over Watson on the basis of 35 U.S.C. § 102(e) is not traversed on the basis of these dates alone.

However, the applicant respectfully traverses the Examiner's rejection on the basis of Watson because it appears the Examiner has misunderstood what Watson actually teaches. According to the Examiner, Watson teaches "a method of identifying a modulator of an immune response comprising a transcription factor binding site and [whereby toxicity either is or is not induced]."

The Watson reference is directed specifically to regulation of a particular gene encoding CD95, the receptor for apoptosis signaling by CD95L. In pertinent part, Watson teaches regulatory polynucleotides that play a role in enhancing and silencing transcription for the CD95

promoter. Column 2, lines 26-28. Watson specifically teaches competitive or antisense strategies to regulate CD95 expression. Column 6, lines 20-39. Watson further teaches the use of CD95 regulatory sequences in reference to regulating expression of genes operatively placed under control of the CD95 regulatory sequences. Column 7, lines 21-26. In other aspects the Watson reference teaches proteinaceous binding molecules (transcription factors) which bind specifically to the CD95 enhancer and silencer regions of the CD95 gene, screening tests related to CD95 expression and its regulation, and identification of CD95 homologs. The last portion of the Watson reference cited by the Examiner (in column 18) teaches that a CD95-specific silencer sequence placed upstream of CD95-specific enhancer elements acts as a dominant negative regulatory sequence, i.e., the CD95 silencer is controlling over the CD95 enhancer elements.

In view of the above, applicant finds that the Watson reference does not teach the use of transcriptional regulatory sequences apart from CD95-specific transcriptional regulatory sequences. As will be evident from above, none of the sequences claimed in the instant application is a CD95-specific transcriptional regulatory sequence.

In summary with regard to the Watson reference, applicant finds the Examiner appears to have misunderstood the actual teachings of the Watson reference, and therefore respectfully requests the Examiner to withdraw her 102(e) rejection over Watson.

Claim Rejections Under 35 U.S.C. § 103(a)

The Examiner rejected claims 8, 10, 13-15, and 18 under 35 U.S.C. § 103(a) in view of Henderson and further in view of Davis (US Patent No. 5,780,448). Claims 8, 10, 13-15, and 18 are canceled. The Examiner appears to be making a single rejection based on the combination of the two references.

Applicant finds that the rejection is improper because the Examiner has failed to make a prima facie case for rejecting the claims under 35 U.S.C. § 103(a). The Examiner has failed to make a prima facie case for rejecting the claims under 35 U.S.C. § 103(a) because the Examiner has misinterpreted the Henderson reference, as previously noted. Combining Henderson with Davis, therefore, does not teach the invention. Applicant therefore respectfully requests the Examiner to withdraw her rejection under 35 U.S.C. § 103(a).

Sequence Compliance

Included herewith are a substitute Sequence Listing, substitute computer readable form (CRF) copy of the Sequence Listing, and an accompanying statement under 37 C.F.R. § 1.821(g). These are submitted in response to the specific request of the Examiner.

Support for Newly Presented Claims 24-39

Claim 24 is directed to a pharmaceutical composition comprising at least one polynucleotide comprising a sequence of a binding site for a transcription factor, the polynucleotide comprising a sequence selected from among SEQ ID NOs:8-14, 16, 17, and 19-23, and a pharmaceutically acceptable carrier and/or diluent. Support for this claim can be found on page 7, lines 20-25; page 17, lines 5-6 (SEQ ID NO:10); and page 25, lines 3-8, 10, 11, and 13-17 (remaining SEQ ID NOs).

Claim 25 adds the limitation that the composition further comprises an antigen, and claim 27 further specifies the antigen to be selected from peptides, polypeptides, proteins, polysaccharides, steroids, tumor cell antigens, and tumor cells. Support for claim 25 can be found on page 5, lines 15-17. Support for claim 27 can be found on page 12, lines 16-18 (peptides, polypeptides, steroids, and tumor cells); page 12, line 30 (tumor antigen); page 6, lines 11-13 (proteins and polysaccharides). The term "antigen" is defined broadly to mean a molecule that can elicit an immune response (beginning at the bottom of page 5). It is well known in the art that peptides, polypeptides, proteins, polysaccharides, steroids, tumor cell antigens, and tumor cells all fit this definition as antigens.

Claim 26 contains the limitation that the polynucleotide contains at least one phosphorothioate linkage. Support for this claim can be found at page 12, line 4.

Claim 28 specifies that the binding site for a transcription factor is a binding site for a transcription factor of a cytokine. Support for this claim can be found on page 11, lines 1-2. Claim 29 further specifies the sequence of the binding site for a transcription factor of a cytokine is SEQ ID NO:9 (related to IL-13) or SEQ ID NO:10 (related to IL-12). Support for this claim can be found on page 25, line 4, and on page 17, lines 5-6.

Claim 30 is directed to a method of modulating an immune response, involving contacting an immune cell with an antigen and at least one polynucleotide which comprises a sequence of a binding site for a transcription factor, the polynucleotide comprising a sequence selected from among SEQ ID NOs:8-14, 16, 17, and 19-23, wherein the polynucleotide is

capable of modulating the immune response to the antigen. Support for this claim can be found throughout the specification, including, for example, page 14, line 12 through page 15, line 14, and in the Examples.

Claim 31 relates to types of antigens, as discussed above.

Claim 32 relates to the polynucleotide comprising at least one phosphorothioate linkage, as discussed above.

Claim 33 specifies that the modulating is selected from among breaking immune tolerance, regulating Th1/Th2 helper cell responses, switching immunoglobulin classes, treating autoimmune diseases, and inducing tolerance. Support for this claim can be found as follows: breaking immune tolerance, page 14, lines 24-26, and page 26, line 27; regulating Th1/Th2 helper cell responses, page 15, line 2; switching immunoglobulin classes, on page 23, lines 13-14, page 15, lines 4-7, and page 18, lines 6-9; treating autoimmune diseases, page 15, lines 12-14 and page 12, line 31; inducing tolerance, page 12, line 31, page 15, lines 9-12, and page 17, lines 19-25.

Claim 34 specifies that the polynucleotide is capable of inducing a cytolytic T cell response, and claim 35 further specifies that the polynucleotide sequence is selected from among SEQ ID NOs:8-10, 12, 16, 19, and 21-23. Support for these claims can be found on page 19, lines 29-30, Figure 1, and Example 5.

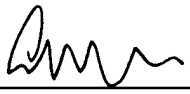
Claim 36 specifies that the polynucleotide is capable of inducing a Th2 immune response, and claim 37 further specifies that the polynucleotide sequence is selected from among SEQ ID NOs:8, 16, and 19. Support for these claims can be found on page 15, line 2, and Figure 3.

Claim 38 specifies that the polynucleotide is capable of inducing a Th1 immune response, and claim 39 further specifies that the polynucleotide sequence is selected from among SEQ ID NOs:8, 12, 14, 16, 19, 22, and 23. Support for these claims can be found on page 18, lines 1-9, and Figure 3.

Summary

It is believed the claims are now in condition for allowance. Favorable action is earnestly solicited. If for any reason the examiner has any question or would require further information, she is encouraged to contact the Applicant's representative at the number presented below.

Respectfully submitted,



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C1041/7005
September 21, 2000
X09/21/2000